

py-oopsi: the python implementation of the fast-oopsi algorithm

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Abstract

Fast-oopsi was developed by joshua vogelstein in 2009, which is now widely used to extract neuron spike activities from calcium fluorescence signals. Here, we propose detailed implementation of the fast-oopsi algorithm in python programming language. Some corrections are also made to the original fast-oopsi paper.

Index Terms

python, fast-oopsi, spikes, calcium fluorescence, connectomics

I. FAST-OOPSI, A BRIEF VIEW

Oopsi, from vogelstein [1], [2], is a family of optimal optical spike inference algorithms. Here, we focus on the development of the fast-oopsi, which was originally published in [2]. We will port the MATLAB implementation to python. Sec II, III, IV, V and VI are digests from the original paper by vogelstein [1].

The python implementation, **py-oopsi**, can be obtained at <https://github.com/liubenyan/py-oopsi>.

II. CALCIUM FLUORESCENCE MODEL

Let \mathbf{F} be a one-dimensional fluorescence trace. At time t , the fluorescence measurement F_t is a linear Gaussian function of the intracellular calcium concentration $[\text{Ca}^{2+}]_t$ at that time:

$$F_t = \alpha[\text{Ca}^{2+}]_t + \beta + e_t, \quad e_t \sim \mathcal{N}(0, \sigma^2) \quad (1)$$

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α determines the scale of the signal, β absorbs the offset. α and β may be learned independently per neuron. The noise e_t is assumed to be i.i.d distributed.

The calcium concentration jumps $A \mu\text{M}$ after each spike and decays back down to baseline $C_b \mu\text{M}$, with time constant τ ,

$$[\text{Ca}^{2+}]_{t+1} = (1 - \Delta/\tau)[\text{Ca}^{2+}]_t + (\Delta/\tau)C_b + An_t, \quad (2)$$

where Δ is the frame interval. The scale A and α , baseline C_b and β are not identifiable, therefore, we may let $A = 1$ and $C_b = 0$ without loss of generality. n_t indicates the number of times the neuron spiked in time t , we may also write it as a delta function δ_t .

Finally, letting $\gamma = (1 - \Delta/\tau)$, we have

$$C_t = \gamma C_{t-1} + n_t \quad (3)$$

and (the filtering model)

$$C[z] = \frac{1}{1 - \gamma z^{-1}} N[z] \quad (4)$$

Note that C_t does not refer to the absolute intracellular concentration, but rather, a relative measure [2]. The simulated calcium trace can be generated if we synthetically generate n_t from a probability distribution. To complete the generative model, we assume spikes are sampled according to a Poisson distribution,

$$n_t \sim \text{Poisson}(\lambda\Delta) \quad (5)$$

where $\lambda\Delta$ is the expected firing rate per bin, Δ is included to ensure that the expected firing rate is independent of the frame rate [2].

III. BAYES MODEL

We aim to find the most likely spike trains $\hat{\mathbf{n}}$ given the fluorescence \mathbf{F} ,

$$\hat{\mathbf{n}} = \arg \max_{n_t \in \mathcal{N}_0, \forall t} p(\mathbf{n}|\mathbf{F}) \quad (6)$$

Using Bayes' rule,

$$p(\mathbf{n}|\mathbf{F}) = \frac{1}{p(\mathbf{F})} \cdot p(\mathbf{F}|\mathbf{n})p(\mathbf{n}) \quad (7)$$

given that $p(\mathbf{F})$ merely scales the results, we rewrite (6) as,

$$\hat{\mathbf{n}} = \arg \max_{n_t \in \mathcal{N}_0, \forall t} p(\mathbf{F}|\mathbf{n})p(\mathbf{n}) \quad (8)$$

and we already have,

$$p(\mathbf{F}|\mathbf{n}) = p(\mathbf{F}|\mathbf{C}) = \prod p(F_t|C_t), \quad (9)$$

$$p(\mathbf{n}) = \prod p(n_t), \quad (10)$$

where,

$$p(F_t|C_t) = \mathcal{N}(\alpha C_t + \beta, \sigma^2), \quad (11)$$

$$p(n_t) = \text{Poisson}(\lambda\Delta) \quad (12)$$

The Poisson distribution penalize sparsity (a sparse prior).

Finally, we have the cost function,

$$\hat{\mathbf{n}} = \arg \max_{n_t \in \mathcal{N}_0} \prod_{t=1}^T \frac{1}{\sqrt{2\pi\sigma^2}} \exp \left\{ -\frac{1}{2} \frac{(F_t - \alpha C_t - \beta)^2}{\sigma^2} \right\} \frac{\exp \{-\lambda\Delta\} (\lambda\Delta)^{n_t}}{n_t!} \quad (13)$$

$$= \arg \max_{n_t \in \mathcal{N}_0} \sum_{t=1}^T -\frac{1}{2\sigma^2} (F_t - \alpha C_t - \beta)^2 + n_t \ln \lambda\Delta - \ln n_t! \quad (14)$$

However, solving for this discretized optimization problem is computational intractable.

IV. APPROXIMATE BAYES FILTER

We can approximate the Poisson distribution with an exponential distribution of the same mean,

$$\frac{\exp\{-\lambda\Delta\}(\lambda\Delta)^{n_t}}{n_t!} \rightarrow (\lambda\Delta) \exp\{-n_t\lambda\Delta\} \quad (15)$$

and consequently,

$$\hat{\mathbf{n}} = \arg \max_{n_t > 0} \sum_{t=1}^T -\frac{1}{2\sigma^2} (F_t - \alpha C_t - \beta)^2 - n_t \lambda\Delta \quad (16)$$

note that $n_t \in \mathcal{N}_0$ has been replaced by $n_t > 0$, since exponential distribution can yield any nonnegative number [2]. The exponential approximation imposes a sparsening effect, and also, it makes the optimization problem concave in \mathbf{C} , meaning that any gradient descent algorithm guarantees achieving **the global maxima** (because there are no local minima).

We may further drop the constraint (nonnegative) by adopting **interior point** method,

$$\hat{\mathbf{n}} = \arg \max_{n_t} \sum_{t=1}^T -\frac{1}{2\sigma^2} (F_t - \alpha C_t - \beta)^2 - n_t \lambda\Delta + z \ln n_t \quad (17)$$

where we add a weighted barrier term that approaches $-\infty$ as n_t approaches zero, by solving for a series of z going down to nearly zero. The goal is to efficiently solve,

$$\hat{\mathbf{C}} = \arg \max_{\mathbf{C}} \sum_{t=1}^T -\frac{1}{2\sigma^2} (F_t - \alpha C_t - \beta)^2 - (C_t - \gamma C_{t-1}) \lambda\Delta + z \ln(C_t - \gamma C_{t-1}) \quad (18)$$

this cost function is twice differentiable, one can use the Newton-Raphson technique to ascend the surface.

V. MATRIX NOTATION AND THE NEWTON-RAPHSON SOLVER

To proceed, we have

$$\mathbf{MC} = \begin{bmatrix} -\lambda & 1 & 0 & 0 & \cdots & 0 \\ 0 & -\lambda & 1 & 0 & \cdots & 0 \\ \vdots & \ddots & \ddots & \ddots & \ddots & \vdots \\ 0 & \cdots & 0 & -\lambda & 1 & 0 \\ 0 & \cdots & 0 & 0 & -\lambda & 1 \end{bmatrix} \begin{bmatrix} C_1 \\ C_2 \\ \vdots \\ C_{T-1} \\ C_T \end{bmatrix} = \begin{bmatrix} n_1 \\ n_2 \\ \vdots \\ n_{T-1} \end{bmatrix} \quad (19)$$

\mathbf{M} is a $(T-1) \times T$ matrix. Now letting $\mathbf{1}$ be a $(T-1) \times 1$ column vector, $\boldsymbol{\lambda} = (\lambda\Delta)\mathbf{1}$, $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ a T -dimensional vector, \odot to indicate element-wise operations, then ¹

$$\hat{\mathbf{C}} = \arg \max_{\mathbf{MC} \geq \odot \mathbf{0}} -\frac{1}{2\sigma^2} \|\mathbf{F} - \boldsymbol{\alpha}\mathbf{C} - \boldsymbol{\beta}\|_2^2 - (\mathbf{MC})^T \boldsymbol{\lambda} + z \ln_{\odot}(\mathbf{MC})^T \mathbf{1} \quad (20)$$

We instead iteratively minimize the cost function \mathcal{L} (called *post* in our python implementation) where,

$$\hat{\mathbf{C}}_z = \arg \min_{\mathbf{C}} \mathcal{L}, \quad \mathcal{L} = \frac{1}{2\sigma^2} \|\mathbf{F} - \boldsymbol{\alpha}\mathbf{C} - \boldsymbol{\beta}\|_2^2 + (\mathbf{MC})^T \boldsymbol{\lambda} - z \ln_{\odot}(\mathbf{MC})^T \mathbf{1} \quad (21)$$

\mathcal{L} is **convex**, when using Newton-Raphson method to **descend** a surface, one iteratively computes the gradient $\mathbf{g} = \nabla \mathcal{L}$ (first derivative) and Hessian $\mathbf{H} = \nabla^2 \mathcal{L}$ (second derivative) of the argument to be optimized. Then, $\mathbf{C} = \mathbf{C} - s\mathbf{d}$, where s is the step size and \mathbf{d} is the step direction by solving $\mathbf{H}\mathbf{d} = \mathbf{g}$. The gradient and Hessian, with respect to \mathbf{C} , are

$$\mathbf{g} = -\frac{\boldsymbol{\alpha}}{\sigma^2}(\mathbf{F} - \boldsymbol{\alpha}\mathbf{C} - \boldsymbol{\beta}) + \mathbf{M}^T \boldsymbol{\lambda} - z\mathbf{M}^T(\mathbf{MC})_{\odot}^{-1} \quad (22)$$

$$\mathbf{H} = \frac{\boldsymbol{\alpha}^2}{\sigma^2} \mathbf{I} + z\mathbf{M}^T(\mathbf{MC})_{\odot}^{-2} \mathbf{M} \quad (23)$$

s is found via **backtracking linesearches**. \mathbf{M} is bidiagonal, so \mathbf{H} is tridiagonal, $\mathbf{d} = \mathbf{H}^{-1}\mathbf{g}$ can be efficiently implemented in matlab by assuming \mathbf{H} is a sparse matrix. In python, we may use sparse linsolvers (linsolve.spsolve) to efficiently find \mathbf{d} . Once $\hat{\mathbf{C}}$ is obtained, it is a simple linear transform to obtain $\hat{\mathbf{n}}$, via $\hat{\mathbf{n}} = \mathbf{M}\hat{\mathbf{C}}$. We will normalize \mathbf{n} by $\mathbf{n} = \mathbf{n}/\max(\mathbf{n})$ after convergence.

VI. PARAMETERS INITIALIZE AND UPDATE

The parameters $\boldsymbol{\theta} = \{\alpha, \beta, \sigma, \gamma, \lambda\}$ are unknown. We may use pseudo expectation-maximization method, (1), initialize the parameters, (2) recursively computes $\hat{\mathbf{n}}$ and updating $\boldsymbol{\theta}$ given the new $\hat{\mathbf{n}}$ until the convergence is met.

¹contrary to [2], but alike **fast-oopsi.m**, we choose \mathbf{M} as a sparse $T \times T$ matrix, and $\mathbf{1}$ as $T \times 1$ column vector. Therefore we have $n_0 = C_0$, we will correct $n_0 = \epsilon$ after convergence.

The scale of \mathbf{F} relative to \mathbf{n} is arbitrary, therefore, \mathbf{F} is firstly *detrended*, and then *linearly mapped* between 0 and 1.

$$\mathbf{F} = \text{detrend}(\mathbf{F}), \quad \mathbf{F} = (\mathbf{F} - F_{\min}) / (F_{\max} - F_{\min}), \quad (24)$$

Next, because spiking is sparse in many experimental settings, \mathbf{F} tends to be around baseline, β is set to the median of \mathbf{F} . We use median absolute deviation (MAD) and correction factor K , as a robust normal scale estimator of \mathbf{F} where $K = 1.4826$. Previous works showed that the results $\hat{\mathbf{n}}$ and $\hat{\mathbf{C}}_z$ are robust to minor variations in the time constant, we let $\gamma = 1 - \Delta$. Finally, λ is set to 1Hz, which is between baseline and evoked spike rate for data of interest ².

$$\alpha = 1, \quad (25)$$

$$\beta = \text{median}(\mathbf{F}), \quad (26)$$

$$\sigma = \text{MAD}(\mathbf{F}) \cdot K = \text{median}(|\mathbf{F} - \beta|) \cdot K, \quad K = 1.4826 \quad (27)$$

$$\gamma = 1 - \Delta / (1\text{sec}), \quad (28)$$

$$\lambda = 1\text{Hz} \quad (29)$$

Then, given $\hat{\mathbf{C}}$ and $\hat{\mathbf{n}}$, we may (approximately) update $\boldsymbol{\theta}$ by,

$$\hat{\boldsymbol{\theta}} \approx \arg \max_{\boldsymbol{\theta}} p(\mathbf{F}, \hat{\mathbf{C}} | \boldsymbol{\theta}) = \arg \max_{\boldsymbol{\theta}} \ln p(\mathbf{F} | \hat{\mathbf{C}}; \{\alpha, \beta, \sigma\}) + \ln p(\hat{\mathbf{n}} | \lambda) \quad (30)$$

where,

$$\hat{\lambda} = \arg \max_{\lambda > 0} \sum_{i=1}^T [\ln(\lambda \Delta) + \hat{n}_t \lambda \Delta] \quad (31)$$

$$\{\hat{\alpha}, \hat{\beta}, \hat{\sigma}\} = \arg \max_{\alpha, \beta, \sigma > 0} \sum_{i=1}^T \left[-\frac{1}{2} \ln(2\pi\sigma^2) - \frac{1}{2} \left(\frac{F_t - \alpha C_t - \beta}{\sigma} \right)^2 \right] \quad (32)$$

We have (by taking the derivatives and letting them equal zero),

$$\hat{\lambda} = \frac{T}{\Delta \sum_t n_t}, \quad (33)$$

$$\hat{\alpha} = 1, \quad (34)$$

$$\hat{\beta} = \frac{\sum_t (F_t - C_t)}{T}, \quad (35)$$

$$\hat{\sigma}^2 = \frac{\sum_t (F_t - C_t - \beta)^2}{T} = \frac{\|\mathbf{F} - \mathbf{C} - \beta\|_2^2}{T} \quad (36)$$

where $\hat{\lambda}$ is the inverse of the inferred firing rate, $\hat{\alpha}$ can be set to 1.0 because the scale of \mathbf{C} is arbitrary, $\hat{\beta}$ is the mean bias, $\hat{\sigma}$ is the root-mean-square of the residual error.

²corrections to [2]: 1), add detrend to \mathbf{F} , 2), $K = 1.4826$ and it is multiplied (not divided by) $\text{MAD}(\mathbf{F})$.

VII. IMPLEMENTATION OF OOPSI

Matlab implementation is available, here we focus on the python migrant, and correct some typos in [2] as needed. The python code itself explains all, see IV, V, and VI for detailed documentary. Pseudo code can be found in Algo 1. Algo 2 describe the subroutine **MAP**, Algo 3 describe the subroutine **update**.

Algorithm 1 Pseudo code (python) for fast-oopsi

```

1: Initialize parameters P:  $\mathbf{F} = \text{detrnd}(\mathbf{F})$ ,  $\mathbf{F} = (\mathbf{F} - \min(\mathbf{F})) / (\max(\mathbf{F}) - \min(\mathbf{F}))$ ,  $\alpha = 1.0$ ,
    $\beta = \text{median}(\mathbf{F})$ ,  $\lambda = 1.0$ ,  $\gamma = 1 - \Delta$ ,  $\sigma = \text{MAD}(\mathbf{F}) \cdot 1.4826$ ,  $T = \text{len}(\mathbf{F})$ 
2: one-shot Newton-Raphson n, C,  $\mathcal{L} = \text{MAP}(\mathbf{F}, \mathbf{P})$ , see Algo 2.
3: for  $i$  in  $1 \cdots \text{iterMax}$  do
4:   update parameters  $\mathbf{P} = \text{update}(\mathbf{n}, \mathbf{C}, \mathbf{F}, \mathbf{P})$ , see Algo 3.
5:   iterative through n, C,  $\mathcal{L} = \text{MAP}(\mathbf{F}, \mathbf{P})$ ,
6:   let  $\mathcal{L}^{(k)} = \{\mathcal{L}_1, \dots, \mathcal{L}_k\}$ 
7:   if  $|\frac{\mathcal{L}_i - \mathcal{L}_{i-1}}{\mathcal{L}_i}| < \text{ltol}$  or any( $|\mathcal{L}^{(i)} - \mathcal{L}_i|$ )  $< \text{gtol}$  then
8:     break
9:   end if
10: end for

```

VIII. WIENER FILTER (LINEAR REGRESSION, SIMPLE CONVEX OPTIMIZATION)

In the wiener filter, we approximate the Poisson distribution with a Gaussian distribution,

$$p(n_t) \sim \mathcal{N}(\lambda\Delta, \lambda\Delta) \quad (37)$$

then, the MAP estimator yields,

$$\hat{\mathbf{n}} = \arg \max_{n_t} \sum_{t=1}^T \left[-\frac{1}{2\sigma^2} (F_t - \alpha C_t - \beta)^2 - \frac{1}{2\lambda\Delta} (n_t - \lambda\Delta)^2 \right] \quad (38)$$

and its matrix notation,

$$\hat{\mathbf{C}} = \arg \max_{\mathbf{C}} -\frac{1}{2\sigma^2} \|\mathbf{F} - \alpha\mathbf{C} - \beta\mathbf{1}\|_2^2 - \frac{1}{2\lambda\Delta} \|\mathbf{MC} - \lambda\Delta\mathbf{1}\|_2^2 \quad (39)$$

which is **quadratic, concave** in **C**.

Finally, we aim to optimize (minimize, **quadratic, convex** optimization),

$$\hat{\mathbf{C}} = \arg \min_{\mathbf{C}} \mathcal{L}, \quad \mathcal{L} = \frac{1}{2\sigma^2} \|\mathbf{F} - \alpha\mathbf{C} - \beta\mathbf{1}\|_2^2 + \frac{1}{2\lambda\Delta} \|\mathbf{MC} - \lambda\Delta\mathbf{1}\|_2^2 \quad (40)$$

Algorithm 2 Pseudo code of subroutine *MAP*

```

1: Initialize  $\mathbf{n} = 0.01\mathbf{1}$ 
2: Initialize  $\mathbf{C}(z) = 1/(1 - \gamma)\mathbf{N}(z)$ 
3: Initialize  $\lambda = \lambda\Delta\mathbf{1}$ 
4: for  $z = 1.0, z > 1e - 13, z = z/10$  do
5:   calculate  $\mathcal{L}_z$ 
6:   while  $s > 1e - 3$  or  $\|\mathbf{d}\| > 5e - 2$  do
7:     Calculate  $\mathbf{g}, \mathbf{H}$  and  $\mathbf{d} = \text{spsolve}(\mathbf{H}, \mathbf{g})$ 
8:     Find  $s : \mathbf{h} = -\mathbf{n}/(\mathbf{M}\mathbf{d}), s = \min(0.99s[s > 0], 1.0)$ 
9:     Initialize  $\mathcal{L}_s = \mathcal{L}_z + 1$ 
10:    while  $\mathcal{L}_s > \mathcal{L}_z + 1e - 7$  do
11:       $\mathbf{C} = \mathbf{C} + s\mathbf{d}$ 
12:       $\mathbf{n} = \mathbf{M}\mathbf{C}$ 
13:      update  $\mathcal{L}_s$ 
14:      decrease  $s = s/5.0$ 
15:      if  $s < 1e - 20$  then
16:        break
17:      end if
18:    end while
19:  end while
20: end for

```

Algorithm 3 Pseudo code of subroutine *update*

```

1:  $\alpha = 1.0$ 
2:  $\beta = \sum_i (F_i - C_i)/T$ 
3:  $\sigma^2 = \|\mathbf{F} - \alpha\mathbf{C} - \beta\|_2^2/T$ 
4:  $\lambda = T/(\Delta \sum_i n_i)$ 

```

where \mathcal{L} is **convex** in \mathbf{C} . Using Newton-Raphson update, we find $\mathbf{C} = \mathbf{C} - \mathbf{d}$, $\mathbf{H}\mathbf{d} = \mathbf{g}$ and $\mathbf{g} = \nabla\mathcal{L}$, $\mathbf{H} = \nabla^2\mathcal{L}$. The gradient \mathbf{g} and Hessian \mathbf{H} are,

$$\mathbf{g} = -\frac{\alpha}{\sigma^2}(\mathbf{F} - \alpha\mathbf{C} - \beta\mathbf{1}) + \frac{1}{\lambda\Delta} [\mathbf{M}^T(\mathbf{M}\mathbf{C}) + \lambda\Delta\mathbf{M}^T\mathbf{1}] \quad (41)$$

$$\mathbf{H} = \frac{\alpha^2}{\sigma^2}\mathbf{I} + \frac{1}{\lambda\Delta}\mathbf{M}^T\mathbf{M} \quad (42)$$

In the python implementation, we let $\alpha = 1.0$ and $\beta = 0.0$. Pseudo code can be found in Algo 4.

Algorithm 4 Pseudo code (python) for wiener filter

```

1: Initialize  $\mathbf{F} = (\mathbf{F} - \text{mean}(\mathbf{F}))/\max(|\mathbf{F}|)$ ,  $\sigma = 0.1\|\mathbf{F}\|_2$ 
2: Calculate  $\mathcal{L}_0$ 
3: for  $i$  in  $1 \cdots \text{iterMax}$  do
4:   Calculate  $\mathbf{g}$ ,  $\mathbf{H}$  and  $\mathbf{d} = \text{spsolve}(\mathbf{H}, \mathbf{g})$ 
5:   Calculate  $\mathbf{C} = \mathbf{C} - \mathbf{d}$ 
6:   Calculate  $\mathcal{L}_i$ 
7:   if  $\mathcal{L}_i < \mathcal{L}_{i-1} + \text{gtol}$  then
8:      $\mathbf{n} = \mathbf{N}$ 
9:      $\sigma = \sqrt{\|\mathbf{F} - \mathbf{C}\|_2^2/T}$ 
10:  end if
11: end for
12:  $\mathbf{n} = \mathbf{n}/\max(\mathbf{n})$ 

```

IX. SIMULATION RESULTS

We generated synthetic calcium traces with $T = 2000$, $\Delta = 20\text{ms}$, $\lambda = 0.1$, $\tau = 1.5$. Randomized noise were added with 0.2 standard deviation. Py-oopsi and wiener filter are used to reconstruct the spikes from calcium fluorescence, where only Δ is known a prior. The results are shown in Figure 1

REFERENCES

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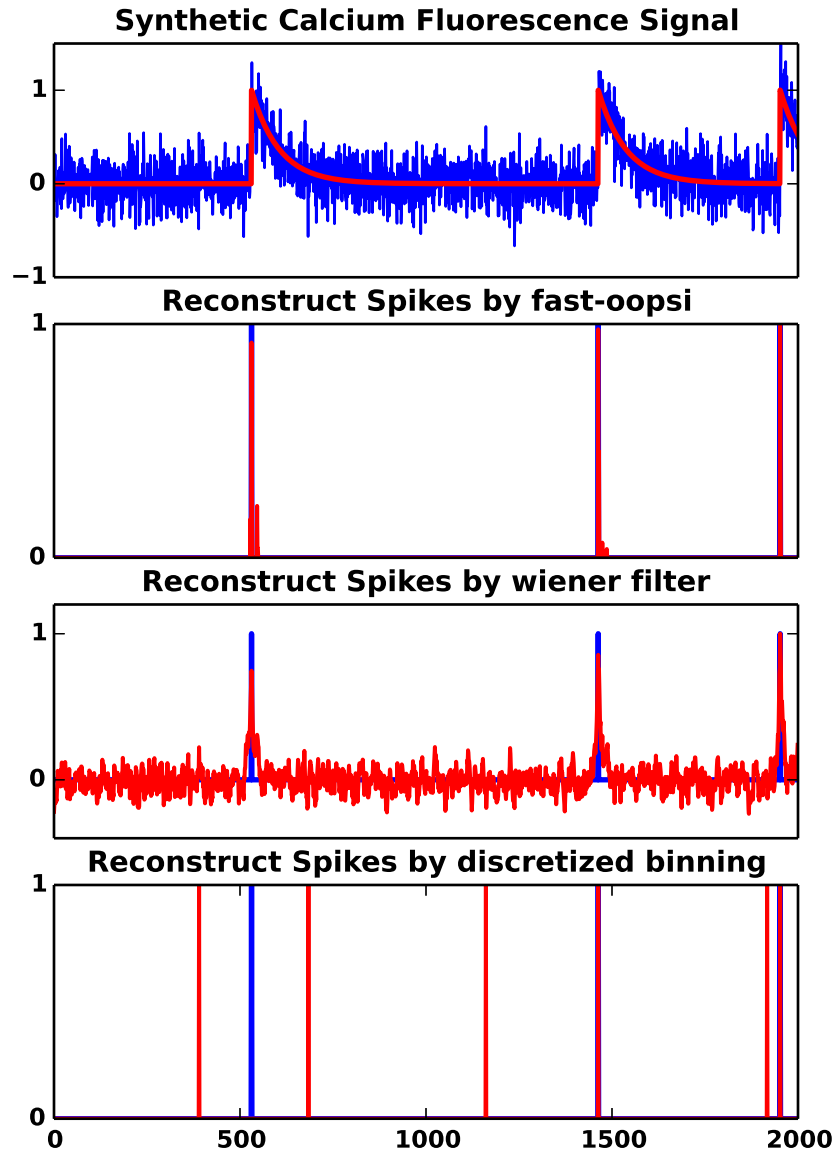


Fig. 1. Reconstruct spikes from calcium fluorescence. (a) The synthetic calcium trace. (b), (c), (d) are reconstructed spikes by py-oopsi, wiener filter and discretized binning, respectively.